

**REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 21-33 were pending in this application when last examined. Claims 14, 18-20, 22, 24, 27, 30 and 31 are withdrawn as non-elected subject matter. Claims 21-33 are currently amended. Support for the amendments can be found in the specification and in the original claims as filed. No new matter has been added.

**CLAIM REJECTIONS - 35 USC § 112, FIRST PARAGRAPH**

At pages 3-4, items 3-5, the Office Action rejects claims 12, 13, 15-17, 21, 23, 25, 26, 28, 29, 32 and 33, under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Currently amended claims 12, 13, 15-17, 21, 23, 25, 26, 28, 29, 32 and 33 address each of the issues noted in the Office Action. Applicants respectfully traverse this rejection.

Regarding item 3, currently amended claim 12 further describes the two components of the biocompatible matrix. The biocompatible matrix comprises: (1) at least one biocompatible polymer of natural origin and (2) grafted chains comprising polymers grafted on the biocompatible polymer of natural origin. Thus, amended claim 12 describes a biocompatible matrix comprising a biocompatible polymer of natural origin with grafted side chains, support for which can be found in the specification,

for example at page 5, lines 24-32, page 7, lines 1-9 and lines 25-29.

Similar to claim 12, currently amended claim 33 further describes another embodiment of the two components of the biocompatible matrix: (1) at least one biocompatible polymer of natural origin and (2) grafted chains comprising compounds having antioxidant properties or properties for inhibiting reactions of degradation of the biocompatible matrix. Thus, amended claim 33 describes a biocompatible matrix comprising a polymer of natural origin with grafted chains comprising compounds having antioxidant properties, support for which can be found in the specification, for example at page 6, lines 4-7, and page 8, lines 19-21.

Regarding the "side chains of natural origin polymers of small size," the Office Action states that the only example of such a side chain is carboxymethyl cellulose and contends that this polymer is not of natural origin. Currently amended claim 12 recites that the grafted chains comprises polymers grafted on the biocompatible polymer. One example of such a grafted chain is carboxymethyl cellulose, support for which can be found in the specification, for example at page 8, lines 17-18, and page 10, lines 7-12.

Regarding item 4, claim 13 describes a biocompatible polymer selected from a group that includes cellulose and carboxymethyl cellulose.

Regarding item 5, claim 33 describes grafted chains comprising compounds having antioxidant properties or properties for inhibiting reactions of degradation of the matrix, the compounds selected from the group consisting of vitamins, enzymes and cyclic molecules. The Office Action acknowledges that these species meet the written description requirement.

In view of the foregoing amendments and remarks, Applicants request reconsideration and withdrawal of this rejection.

**CLAIM REJECTIONS - 35 USC § 112, SECOND PARAGRAPH**

At pages 5-7, items 7-10, the Office Action rejects claims 12, 13, 15-17, 21, 23, 25, 26, 28, 29, 32 and 33, under 35 U.S.C. § 112, second paragraph, as being indefinite. Currently amended claims 12, 13, 15-17, 21, 23, 25, 26, 28, 29, 32 and 33 address each of the issues noted in the Office Action. Applicants respectfully traverse this rejection.

Regarding item 7, each of currently amended claims 12, 13, 15-17, 21, 23, 25, 26, 28, 29, 32 and 33 are directed to a biocompatible matrix, support for which can be found throughout the specification, for example, at page 1, lines 1-2, and page 12, lines 4-5.

Regarding item 8, one of ordinary skill in the art would recognize that a "biocompatible polymer of natural origin" could mean polymers isolated from natural sources and polymers

synthesized in a laboratory. Even laboratory synthesized polymers can be identical to and represent natural origin polymers.

The Office Action also takes issue with the phrase "comprising polymers of natural origin of small size" in claims 12 and 33. This phrase has been deleted from amended claim 12, and this phrase was never recited in claim 33.

The Office Action notes lack of antecedent basis for "number of moles of grafted molecules" in claim 12 and 33. Amended claim 12 recites "number of moles of grafted polymer" and amended claim 33 recites "number of moles of grafted chains." Antecedent basis for these features can be found in the respective claim.

The Office Action takes issue with the ability to clearly calculate the quantity of grafting in claims 12 and 33. Currently amended claims 12 and 33 further clarify the definition for calculating of the quantity of grafting. Support for the calculation can be found in the specification, for example, at page X.

Regarding item 9, the Office Action takes issue with "the grafted matrix" in claims 32 and 33. Each of amended claims 32 and 33 further clarifies the "biocompatible matrix comprising grafted chains."

Regarding item 10, the Office Action takes issue with the phrase "non-polymeric chains having antioxidant properties ..." Currently amended claim 33 further clarifies that the

grafted chains comprise compounds having antioxidant properties, and the compounds are "vitamins, enzymes and cyclic molecules." Support for these compounds can be found in the specification, for example, at page X.

In view of the foregoing amendments and remarks, each of claims 12, 13, 15-17, 21, 23, 25, 26, 28, 29, 32 and 33 satisfies the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

**CLAIM REJECTIONS - 35 USC § 103**

At page 8, item 14, the Office Action rejects claims 12, 13, 17, 32 and 33 under 35 U.S.C. § 103(a) as being unpatentable over NGUYEN (EP 0749982A).

At page 10, item 15, the Office Action rejects claims 12, 13, 16, 23, 29, 32 and 33 under 35 U.S.C. § 103(a) as being unpatentable over NGUYEN in view of RAMAMURTHI (J. Biomed. Mater. Res., 2002).

At page 10, item 16, the Office Action rejects claims 12, 13, 15, 21, 32 and 33 under 35 U.S.C. § 103(a) as being unpatentable over NGUYEN in view of BOLOTIN (PGPub 2003/0224974).

At page 11, item 17, the Office Action rejects claims 12, 13, 16, 23, 29, 32 and 33 under 35 U.S.C. § 103(a) as being unpatentable over NGUYEN in view of BOLOTIN and RAMAMURTHI.

Applicants respectfully traverse each of these rejections.

Independent claim 12 as currently amended is directed to a biocompatible matrix that includes (1) at least one biocompatible polymer of natural origin, cross linked with a cross linking agent selected from the group consisting of epoxides, epihalohydrines and divinylsulfone, and (2) grafted chains comprising polymers grafted on the biocompatible polymer of natural origin, each grafted chain having a molecular weight less than 50,000 Da, wherein the quantity of grafting is from 10% to 40%. Similarly, the biocompatible matrix of independent claim 33 features grafted chains comprising compounds having antioxidant and/or anti-degradation properties.

Such a biocompatible matrix having grafted chains in a quantity of grafting of 10-40% has improved gel resistance against attacks from components (i.e., enzymes and free radicals) of the body in which it is injected, while also providing a gel having a reasonable ejection force. NGUYEN fails to teach or suggest such a biocompatible matrix.

NGUYEN describes grafted polysaccharide compositions grafted with antioxidants, with a quantity of grafting up to 10% but preferably well below this upper limit. The object of grafting in to improve the resistance to radical degradation (see, page 2, lines 37-40). In distinction from NGUYEN, the present application and the claimed matrix has improved

resistance to radical degradation and also resistance to other kinds of degradation (i.e., enzymatic). This is one reason why the amount of grafting (10-40%) is much higher than in NGUYEN.

NGUYEN discloses an upper limit of grafting of 1 to 10 with a preferred grafting between 1 to 100 and 1 to 400. NGUYEN maintains the lower grafting limits in order to maintain an ejection force within reasonable limits and allow injection of the product in to the body.

In contrast to NGUYEN, the presently claimed matrix is highly grafted (10-40%) on a crosslinked polymer. One of ordinary skill in the art would consider that such a dense product resulting from the high amount of grafting in the claimed matrix, the ejection force will not allow the injection of the product in to the body. Indeed, NGUYEN probably recognized this condition by limiting the maximum amount of grafting.

The presently claimed matrix, featuring crosslinked polymer and 10-40% grafting of chains having a molecular weight less than 50kDa, allows a high degree of protection from degradation from both radicals and enzymes. Critically, however, and unexpectedly, the grafting reduces the ejection force compared to a non-grafted polymer. As detailed in Table 1 and Table 2, the cross linked and grafted gels within the scope of the claims have a force of ejection less than that of cross linked gels. As a result, the presently claimed matrix has improved injectability (see, pages 17-18).

For at least these reasons, NGUYEN fails to teach or suggest, and fails to render obvious, a biocompatible matrix having the combination of features recited in claim 12 and in claim 33. Claims 13, 17 and 32 each depends from claim 12 and for at least the same reason also would not have been rendered obvious. Accordingly, Applicants request reconsideration and withdrawal of the rejection over NGUYEN.

In further regard to the remaining rejections, BOLOTIN and RAMAMURTHI, alone or in combination, fail to remedy the deficiencies of NGUYEN. RAMAMURTHI and BOLOTIN fail to teach or suggest a biocompatible matrix having the combination of features recited in claim 12 and in claim 33. Thus, the combination of NGUYEN, RAMAMURTHI and BOLOTIN fails to render obvious claims 12, 13, 15-17, 21, 23, 29, 32 and 33. Accordingly, Applicants request reconsideration and withdrawal of each of the rejections over NGUYEN in view of RAMAMURTHI, NGUYEN in view of BOLOTIN, and NGUYEN in view of RAMAMURTHI and BOLOTIN.

#### **CONCLUSION**

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.



If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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